REMARKS

In the Office Action of November 26, 2006 (Paper No. 11262005), claims 1 and 14 were rejected under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the written description requirement. The prior rejections of claims 1-7, 9, 10, 13-18, 20, 21, and 24, and of claims 8, 19 and 25 – 28 pursuant to 35 U.S.C. 103(a) have been continued.

Concerning the Claim Rejections – 35 USC § 112

The Examiner has argued that the range of "less than 0.4 units" as recited in claims 1 and 14 does not meet the written description requirement since that range has no lower limit and would cause the claims to literally read outside the ranges recited in the specification. In response, Applicant does agree that this language could be interpreted to read on ranges outside of those literally recited in the specification. However, Applicant also points out that the subject matter of a claim need not be described literally or "*in haec verba*" in order for the specification to satisfy the description requirement. See e.g., *Staehelin v. Secher*, 24 USPQ2d 1513, 1519 (BPAI 1992). "The question, therefore, is whether the originally filed application would have reasonably conveyed to a person of ordinary skill in the art that applicants invented the subject matter later claimed by them including the limitations in question." *Id.*

Given then that the relevant inquiry is dependant on a consideration of a person of ordinary skill in the art, Applicant has clarified claims 1 and 14 to recite a lower limit of "about .01 units" for the recited range. As the Examiner is doubtless aware, the use of the term "about" does not render the claims indefinite. See e.g., *Modine Mfg. Co. v. U.S. Intern. Trade Comm'n*, 75 F.3d 1545, 1554 (Fed. Cir. 1996)("Although it is rarely feasible to attach a precise limit to 'about' the usage can usually be understood in light of the technology embodied in the invention."); *W.L. Gore & Assocs., Inc. v. Garlock, Inc.*, 721 F.2d 1540, 1557 (Fed. Cir.

1983)(descriptive term "about," when used to describe ranges in a patent, does not render a claim indefinite).

By clarifying the claims in this matter Applicant fundamentally rejects any notion that it has limited itself to an absolute lower limit of .01 units. Instead, Applicant has used the clear teaching of the specification to set a lower limit for the recited range that includes not only .01 units, but also such range of units below that number as would be understood by one of skill in the art based upon the specification.

Regarding the Rejection of Claims 1-7, 9, 10, 13-18, 20, 21 and 24 Under 35 U.S.C. §103(a) as Obvious Over Trese et al. (Ophthalmology)

Applicant hereby incorporates by reference the remarks set forth in the prior Appeal Brief with respect to independent claim 1, independent claim 14 and Trese et al. (Ophthalmology).

The Examiner's rejection of the claims is based, in its entirety, on the unsupported conclusion that "it is well known in the medical field art to vary the does size that will be injected into a patent" and "[t]his concept is well known in the research art." However, nowhere has the Examiner pointed to an objective teaching in the prior art that would permit one of skill in the art to conclude that the claimed process of delivering a dose of plasmin is obvious. Therefore, the rejection must be withdrawn.

The Examiner may not, because of doubt that the invention is patentable, resort to speculation, unfounded assumption or hindsight reconstruction to supply deficiencies in the factual basis for the rejection. See *In re Warner*, 379 F.2d 1011, 1017, 154 USPQ 173, 177 (CCPA 1967), *cert. denied*, 389 U.S. 1057 (1968). Rather, in determining obviousness, "the [E]xaminer can satisfy the burden of showing obviousness of the combination 'only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary

skill in the art would lead that individual to combine the relevant teachings of the references.'" *In re Lee*, 277 F.3d 1338, 1343, 61 USPQ2d 1430, 1434 (Fed. Cir. 2002), citing *In re Fritch*, 972 F.2d 1260, 1265, 23 USPQ2d 1780, 1783 (Fed. Cir. 1992). "Mere denials and conclusory statements, however, are not sufficient to establish a genuine issue of material fact." *Dembiczak*, 175 F.3d at 999-1000, 50 USPQ2d at 1617, citing *McElmurry v. Arkansas Power & Light Co.*, 995 F.2d 1576, 1578, 27 USPQ2d 1129, 1131 (Fed. Cir. 1993). Here, the Examiner is plainly using hindsight reconstruction to concluded that the present invention is obvious over Trese et al. (Ophthalmology).

The claimed invention is not obvious over Trese et al. (Ophthalmology) since the separation of the vitreous from the dissimilar retinal tissue is a less effective vitreal treatment, as compared to the claimed invention. The liquefaction of the vitreous represents not only a separation, but a dissolution of the gelled vitreous. There is no objective teaching or contemplation in Trese et al. (Ophthalmology) that plasmin injected into a subject eye is able to induce vitreous liquefaction. Therefore, this higher level of performance as recited in claim 1 and claim 14 is not obvious in light of Trese et al. (Ophthalmology).

The notion that one skilled in the art would be motivated to deliver a dose of plasmin in the claimed range into a vitreous body of a subject human eye and incubate the plasmin for a predetermined amount of time *to create a liquefied vitreous* is also not provided by the prior art of Trese et al. (Ophthalmology). Indeed, the only motivation for the described process is found in the pending application and the Examiner's hindsight reconstruction based upon that description is improper. Therefore, independent claim 1, independent claim 14 and those claims that depend therefrom are patentable over Trese et al. (Ophthalmology).

Regarding the Rejection of Claims 8, 19 and 25-28 Under 35 U.S.C. §103(a) as Obvious Over Trese et al. (Ophthalmology) and Further in View of Trese et al. (American).

Applicant incorporates by reference the above remarks with regard to Trese et al. (Ophthalmology).

Claims 8, 19 and 25-28 are allowable on the basis of dependency from an allowable base claim. Further, the prior art reference combination failed to yield the claimed invention of claims 8, 19 and 25-28 not only for the reasons cited above, but also based on the fact that Trese et al. (Ophthalmology) and further in view of Trese et al. (American) failed to teach, or provide a motivation for, vitreous liquefaction. Instead, those references only would indicate to one of skill in the art that vitreoretinal separation is possible.

In the case of *In re Wesslau*, the Court of Customs and Patent Appeals cautioned that "it is impermissible within the framework of section 103 to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art." *In re Wesslau*, 353 F.2d 238, 241, 147 USPQ 391, 393 (CCPA 1965). More recently, the Federal Circuit held that a single line in a prior art reference taken out of context and relied upon with the benefit of hindsight is impermissible to show obviousness. Instead, a reference should be considered as a whole, and portions arguing against or teaching away from the claimed invention must be considered. *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve, Inc.*, 796 F.2d 443, 448, 230 USPQ 416, 419-420 (Fed. Cir. 1986). The Federal Circuit has also noted that "[a] reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction

divergent from the path that was taken by the applicant." *In re Gurley*, 27 F.3d 551, 553, 31 USPQ2d 1130, 1131 (Fed. Cir. 1994).

Trese et al. (American) is deficient in that it lacks a teaching or motivation for the creation of a liquefied vitreous. Trese et al. (American), like Trese et al. (Ophthalmology), pertained to macular holes and only teaches the creation of a traumatic posterior vitreous separation. While both references admittedly teach the creation of a vitreoretinal separation, also detailed as a posterior vitreous detachment (PVD), both references alone or in combination fail to contemplate or teach a higher level of effect, namely vitreous liquefaction as compared to vitreoretinal separation.

In addition, Trese et al. (American) teaches away from the present invention. In the discussion section of Trese et al. (American) it states:

> The dose of 0.4 IU of autologous plasmin enzyme, which seems optimal for producing a PVD in humans, does not show the *reliable* liquefaction of vitreous that was seen in animals. This suggests to us that a vitreous cutter is still necessary to safely remove the partially liquefied vitreous, making space for gas used in the postoperative management of stage 3 macular holes. We believe that this study demonstrates that it is possible to achieve spontaneous posterior vitreous separation and closure of macular holes in the human eye but that liquefaction of the vitreous gel is *variable* in human eyes at the dose of 0.4 IU. (*emphasis added*)

A key point to be gleaned from the above passage is that Trese et al. (American) could not secure reliable results at a dose of 0.4 IU and, as a result, the use of vitreous cutter remained necessary. The clear reason for the unreliability of the dose at 0.4 IU was that liquefaction was found by Trese et al. (American) to be variable in human eyes at that dose. Stated differently, at the time of the invention one of ordinary skill in the art would have modified the teachings of Trese et al. (Ophthalmology) and Trese et al. (American) by varying the dose to *greater* than 0.4 IU of

autologous plasmin for reliable liquefaction of the vitreous in humans, *not less than* 0.4 IU since 0.4 units was found not to work. Therefore, based on these comments in the prior art, it is clear that one "of ordinary skill [in the art], upon reading [this] reference, ... would be led in a direction divergent from the path that was taken by the applicant." *In re Gurley.*

It is also of interest to note that one with apparent ordinary skill in the art did comment on the "six potential goals" of the "use of plasmin intravitreally during macular hole surgery" (see Discussion by Jay S. Duker, M.D. included within Trese et al. (American)). These six potential goals outlined by one skilled in the art were: 1) reducing the suction levels and therefore the traction on the retina when surgically inducing a PVD; 2) minimizing the need for delicate and difficult dissection of the internal limiting membrane; 3) decreasing operating time; 4) improving visual outcome; 5) decreasing complications; and 6) possibly enabling macular hole surgery to become an office-based procedure. The reduced "suction levels" mentioned above in goal #1 was discussed in the context of the plasmin being used because of "its activity on laminin and fibronectin, two molecules responsible to a large degree for the adhesion between the anterior retina and the posterior hyaloid." Nowhere is it mentioned, or even suggested, that the use of less than 0.4 IU of plasmin could have a potential for liquefaction of a human vitreous. In other words, it was not obvious to this individual skilled in the art to combine the teaching of Trese et al. (Ophthalmology) and Trese et al. (American) to deliver a dose of plasmin of less than 0.4 units in a volume of about 0.1 cubic centimeters into a vitreous body of a human eye and incubate the plasmin in the vitreous body for a predetermined amount of time *to create a liquefied vitreous.*

Therefore, in view of the above, it is apparent that one skilled in the art would not be motivated by the combination of Trese et al. (Ophthalmology) in view of Trese et al. (American).

to deliver a dose of plasmin in the claimed range into a vitreous body of a human eye and incubate the plasmin in the vitreous body for a predetermined amount of time to create a liquefied vitreous. The only motivation to perform the process disclosed in the present invention is found in the pending application and hindsight reconstruction is improper. Therefore, claims 8, 19 and 25-28 are patentable over Trese et al. (Ophthalmology) and further in view of Trese et al. (American).

Reply to Examiner Response to Arguments

Applicant now responds to the Examiner's Response to Arguments as set forth on Pages 5 –6, paragraph 7 – 13, of Paper No. 11262005.

First, as mentioned above, to the extent that Trese et al. (Ophthalmology) and Trese et al. (American) disclosed a "method of liquefying the eye with a plasmin", neither reference disclosed a process to deliver a dose of plasmin using the range as now claimed *to create a liquefied vitreous*. Further, Trese et al. (American) clearly teaches away from the present invention.

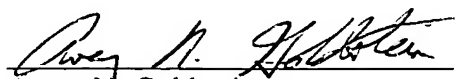
Regarding the Examiner's argument that it would be obvious to vary the concentration and size of a dose, Applicant respectfully queries "Obvious in light of what?" As mentioned above, the *objective* teaching of the prior art either does not teach or, more notably, teaches away from the claimed process. Therefore, to the extent that one of skill in the art would be at all motivated to experiment with dosages, the prior art of record confirms that such experimentation would focus on finding a *reliable* dosage above, not below, 0.4 units.

Regarding criticality, the Examiner argued that "[t]here is no evidence in the specification that 0.4 IU is critical for the invention to work. Applicant respectfully disagrees and points to page 5, line 5 of the Specification, which specifically recited 0.4 units.

Finally, the Examiner has cited to *In re Aller* in support of the proposition that "[w]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." Applicant, however, respectfully submits that this passage from *In re Aller* refers to an attempt to claim an optimum range within a broader range (i.e., a general condition) that is itself cited in the prior art. *See e.g., In re Swain and Adams*, 70 USPQ 412 (CCPA 1946)(cited by *In re Aller*)(wherein the prior art disclosed an ambiguous range, the upper reaches of which could not be predicted but which were nevertheless sufficient to disclose the claimed range.)

In the present application, Applicant is not attempting to claim a range within the "general conditions" taught by the prior art. Indeed, as mentioned above, the range now claimed for the delivery of a dose of plasmin is completely outside of any range recited by the prior art. Therefore, reconsideration and allowance of the claims is respectfully solicited.

Respectfully submitted,



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